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FACILITATION OF SEIZURES IN LIMBIC EPILEPTIC RATS BY COMPLEX 1 MICROTESLA MAGNETIC FIELDS[1]

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Summary.—On three separate sessions 24 male rats with histories of limbic epilepsy were exposed to 10 temporal configurations for 5 min. each of one of two patterns of magnetic fields. Their intensities averaged about 1 microTesla (μT). The numbers of Level 5 (Racine) seizures, inferred by the rat's rearing, rapid forelimb clonus, and falling, were statistically more frequent for the frequency-modulated (Thomas) pattern when its pixel duration and interstimulus presentation were 3 msec. The effectiveness of this temporal configuration was replicated in a second within-subjects experiment ($n = 9$) that directly compared the numbers of seizures during exposures to each of the two patterns and to a sham-field. These results suggest that brains with sensitive limbic systems might respond to weak magnetic fields, generated from multiple overlapping fields from communication and computer systems whose temporal derivatives emerge as complex sequences with pixel durations within the millisecond range.

The brain can be conceptualized as a neuromatrix composed of clusters of several millions of neurons and glial cells that interact in highly organized, synchronous modes (Kelso, 1995). The time-varying electromagnetic interactions within these large functional spaces would be constrained by the temporal parameters that define information. This information would emerge within and be mediated through the complexity of these electromagnetic interactions. Highly synchronous redundant fields, such as 60-Hz sine waves or square waves, would contain minimal neuronal information because they do not even approximate natural neuronal activity. The neuronal effectiveness of these symmetrical, simple patterns would be more dependent upon their intensities and long durations of exposure.

We have assumed that access to the neuromatrix by external electromagnetic stimuli will be affected primarily by the point-to-point (pixel) durations of the variations in the intensities of the applied magnetic fields. Once accessed, the information to which the brain could respond might be contained within the complex, asymmetrical temporal patterns of the amplitudes of these optimal durations. Intensity of the averaged applied magnetic field, once a threshold had been achieved, would be least important. The analogy would be conversation. Once the auditory threshold has been achieved, one

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can whisper or scream the sentences. The sentences, not the intensity of the vocalization, contain most of the information.

During most electrophysiological states within the normal brain the dominant role of inhibitory processes between neurons would be expected to diminish any effects of magnetic fields penetrating brain space from exogenous sources. When the activities of inhibitory interneurons are attenuated, the effects of applied magnetic fields might be amplified sufficiently to be observed as consistent behavioral patterns. Magnetic sequences with structures that approach the complexity and temporal characteristics of neurogenic patterns of activity would be most effective.

Rats in which seizures have been induced by lithium and pilocarpine exhibit significant changes in the structural organizations of their brains. After a quiet period, between a few days and 40 days after the initiation and termination of status epilepticus, spontaneous seizures occur intermittently throughout the rat's lifetime (Cavalheiro, Leite, Bortolotto, Turski, Ikonomidou, & Turski, 1991). The durations of these very obvious seizures, primarily rearing, rapid forelimb clonus, and falling, are of approximately 30 sec. to 1 min. duration (Persinger, Bureau, Kostakos, Peredery, & Falter, 1993), are coincident with electrical seizures as verified by concurrent electroencephalographic measures (Cavalheiro, *et al.*, 1991), and are identical to Racine's Level V seizures induced by kindling (Racine, 1972).

The occurrence of these conspicuous overt seizures increases during 24-hr. periods when the average global geomagnetic activity exceeds 20 nT (Persinger, 1995). This phenomenon can also be simulated by experimental imitation (for about one hour) of geomagnetic activity during nocturnal periods (Michon & Persinger, 1997). Considering the sensitivity of rats with limbic epilepsy to weak magnetic fields, we hypothesized that rats with labile limbic systems might be employed as sensitive "biological indicators" for the effects of artificial electromagnetic fields, such as those generated near electronic equipment, upon the brain. The intensities of these magnetic fields within the exposure area for most human activities range between 100 nT (1 mG) and 10 microT (100 milligauss).

The general goal of our research is to by-pass classical sensory modalities and influence the brain directly. We assume that the brain itself is a "receptor" with as yet unspecified characteristics. One specific goal of our research is to discern the optimal temporal parameters of weak magnetic fields that can affect brain function. The purpose of the present experiment was to discern which of two temporal patterns of magnetic fields, frequently employed by us to study memory, would increase the occurrence of these conspicuous, stereotyped displays of overt forelimb clonus in epileptic rats.

We reasoned that the time constant of individual neurons, which is on the order of about 1 msec. (Koester, 1991), would be reflected within the

property of the emergent fields generated by (and within which are immersed) the larger aggregates of neurons. Consequently we selected pixel values, the durations in real time for each of the (voltage) values that compose the hundreds of values of the complex patterns, to be 1 msec., 2 msec., and 3 msec.

Method

Subjects

In two separate experiments, a total of 33 ($n=24$ and 9) male Wistar rats were employed as subjects. Between 90 and 100 days of age the rats had been injected subcutaneously with 3 mEq/kg of lithium chloride followed 4 hr. later by a subcutaneous injection of 30 mg/kg of pilocarpine. Within 30 min. after the onset of status epilepticus, each rat was injected subcutaneously with 25 mg/kg of acepromazine to promote survival (Persinger, *et al.*, 1993).

Procedure

After the recovery from the induction of the seizures all rats were returned to standard wire cages. Food and water were available *ad libitum* throughout the course of the experiments. The room temperature was controlled and ranged between 20 and 21°C. The light–dark cycle was 12 hr.:12 hr. and the local day began at 0800 hr. Each experiment was completed separately by one of the authors. The times between the induction of the seizures and the experiments were 270 days (Exp. I) and 40 days (Exp. II).

For both experiments each rat was housed singly in plastic cages and placed in experimental rooms that contained the same lighting schedules and temperatures as the maintenance rooms. In two blocks (Exp. I), the cages were placed within one of two identical (6 cages per rack) coils. Each rack was surrounded by electrical wire (72 turns). The two racks were orthogonal to each other and separated by 2 m to minimize any mutual induction. Direct measurement indicated the background field of one coil while the other was activated was less than 10 nT (the limits of the sensor). For Exp. II, a within-subject design, all nine rats were maintained in the same rack. In both experiments the cages were never removed or disturbed except when the corncob bedding was replaced every 10 days.

Once every two or three days between 1300 and 1600 hr. (Exp. I) or once every four or five days between 1800 hr. and 1900 hr. (Exp. II), the rats were exposed to the treatments. In Exp. I, a total of 12 rats were always exposed to the burst-firing pattern field while another 12 rats were always exposed to the Thomas pattern. In Block 1 the rats from a given treatment were housed in one coil while in Block 2 the rats from a given treatment were housed in the other coil. Only one pattern was administered on any

given day. In Exp. II, the same nine rats were exposed to the Thomas pattern as well as to the burst-firing pattern and a sham field. Pictures of the shapes of these patterns have been published elsewhere (Richards, Persinger, & Koren, 1993; Thomas, Kavaliers, Prato, & Ossenkopp, 1997).

The magnetic fields from these patterns were generated from a personal computer (XT) by converting each of the numbers, between 0 and 255, that composed the 890 pixel sequences for the Thomas pattern and the 290 pixel sequences for the burst pattern into voltage. This was completed through a custom-constructed digital-to-analogue converter. The changing voltage and concomitant current then generated the magnetic fields. The field strengths within the exposure areas were affected by the proximity to the edge of the coil and by the pixel duration. For both patterns, the averaged field strengths for the 1-msec., 2-msec., and 3-msec. pixel durations were .8 microT, .5 microT, and .3 microT, respectively, within the cages in the middle of the coil and 1.3 microT, 0.9 microT, and 0.6 microT in the cages closest to the edge of the coil. The shape and presence of the patterns were verified by recording with a Beckman electroencephalograph the inductions within a small solenoid (modified reed switch containing a small nail) placed within the coils. Digital plotting of the strip chart pattern with the actual series of numbers between 0 and 255 from the computer program gave correlation coefficients (r) of .86, .90, and .93 for the 1-, 2-, and 3-msec. pixel durations, respectively.

For Exp. I the 24 treated rats were exposed to each of the following parameters, composed of interstimulus durations and pixel durations (in parentheses) for 5 min. each. The 10 pulse forms had the following temporal structures: 3,000 (3) msec., 300 (3) msec., 30 (3) msec., 3 (3) msec., 2,000 (2) msec., 200 (2) msec., 20 (2) msec., 1,000 (1) msec., 100 (1) msec., and 10 (1) msec. The interstimulus time was the time between the presentation of the whole pattern while the pixel duration was the time the voltage value (between 0 and 255) or a pixel was generated before the next point value was generated. These parameters were applied through the Thomas pattern and the burst pattern on six separate days (three days per pattern). The numbers of seizures displayed for each rat were totalled.

On the bases of the results from Exp. I, the nine rats in Exp. II were exposed for 10 min. per day to either the Thomas or burst pattern with 3-msec. interstimulus and 3-msec. pixel durations or to sham fields. This sequence was repeated three times (a total of nine exposures) for each rat. For the sham-field condition the equipment was activated but the cable between the digital-to-analogue converter and coil was disconnected. The total numbers of seizures displayed by each rat could range between 0 and 3 (maximum number of exposures to a specific parameter).

Results

Two-way analysis of variance with one level repeated (the 10 temporal configurations) and one not repeated (burst-firing vs Thomas pattern) demonstrated a statistically significant difference between the two patterns ($F_{1,22} = 3.12$, $p < .01$, $\eta^2 = 18\%$) for the numbers of observed overt seizures. The interaction between the pattern of the field and the configurations was also statistically significant ($F_{9,194} = 1.79$, $p < .05$, $\eta^2 = 11\%$), while the difference between the configurations was not significant statistically $F_{9,194} = 1.46$, $p > .05$). *Post hoc* analysis, employing paired t tests, indicated that the major source of the interaction between the field patterns and the temporal configurations was due to the greater numbers of seizures displayed by the group exposed to the Thomas pattern when its pixel duration was 3 msec.

The means and standard deviations for the numbers of rats per session that displayed overt seizures during the presentations of the various field parameters for those exposed either to the Thomas pattern or to the burst-firing pattern are shown in Table 1. Nonparametric (Kruskal-Wallis) tests verified that more seizures were displayed by the rats exposed for 5 min. to the Thomas pattern when the pixel duration was 3 msec. and the interstimulus interval was either 3,000 msec. ($\chi^2 = 4.92$, $p < .05$) or 3 msec. ($\chi^2 = 6.57$, $p = .01$) compared to the burst-firing pattern.

TABLE 1

Means and Standard Deviations For Number of Rats Displaying Seizures During Successive 5-min. Exposures to Either Burst-firing ($n = 12$) or Thomas ($n = 12$) Patterns as a Function of Pixel Durations (in msec.) and Interstimulus Intervals (in msec.)

Pixel Duration	Interstimulus Interval	Field Pattern			
		Burst-firing		Thomas	
		M	*SD*	*M*	*SD*
3	3000	.0[a]	.0	.6[b]	.7
3	300	.4	.5	.3	.4
3	30	.5	.5	1.0	.9
3	3	.0[a]	.0	1.0[b]	1.1
2	2000	.5	.8	.6	.9
2	200	.4	.7	.6	.7
2	20	.0	.0	.3	.4
1	1000	.8	1.0	.3	.4
1	100	.8	.9	.5	.5
1	10	.1	.3	.3	.4

[a] vs [b] $p < .01$.

The means and standard deviations for the numbers of seizures per session for Exp. II for the rats that received the Thomas pattern, the burst pattern (both patterns with 3-msec. pixel and interstimulus durations), and the sham condition, are shown in Table 2. Paired t tests indicated that the

rats displayed significantly (all dfs = 8) more seizures when exposed to the Thomas pattern compared to the sham field ($t = 2.35$, $p < .05$) but not to the burst pattern ($t = 1.81$). The difference between the numbers of seizures during exposure to the sham field or to the burst pattern was also not significant ($t = .48$) statistically.

TABLE 2
MEANS AND STANDARD DEVIATIONS FOR NUMBERS OF SEIZURES PER 10-MIN. EXPOSURE TO EITHER SHAM, BURST PATTERN, OR THOMAS PATTERN FIELDS

Measure	Sham Field	Burst Pattern	Thomas Pattern
M	.2[a]	.3[A]	.6[B]
SD	.3	.3	.3

[a vs b] $p < .05$.

DISCUSSION

The purpose of this study was not to associate complex electromagnetic fields with the induction of epilepsy but to employ animals with this proclivity as biological monitors of the potential electromagnetic changes that might occur within sensitive brains of human beings exposed to weak complex magnetic fields. Our results suggest that rats with limbic epilepsy are sensitive to ambient complex magnetic fields whose amplitudes are within the range of those emitted by computer systems and other electronic devices. That the facilitation of seizures during the presentation of the Thomas pattern compared to the burst pattern in Exp. I was an artifact of the elevated field strength associated with the pixel duration is unlikely because the 3-msec. pixel durations were associated with lowest of the field intensities generated within the exposure area.

The specificity of the influence of the Thomas pattern with pixel durations of 3 msec. and interstimulus presentations of 3 msec. was suggested by the replication study. In that experiment another group of rats were exposed to this pattern, the burst pattern, or to a sham field on three separate occasions (nine exposures). We suggest that pixel durations of 3 msec. may be required to overcome the intrinsic impedance and reluctance within neural tissue of rats with this particular expression of limbic epilepsy. Very short pixel durations associated with the direct electromagnetic signals from telecommunications (which would be within the nanosecond and microsecond ranges) would not be expected to access the activity of neural networks directly. Instead, the temporal integration and averaging of these fields would either damage the neuronal networks due to thermal effects or be concealed as "neutral" shifts in steady potentials. The latter would be analogous to adding a constant to a series of numbers and would minimally affect the relative temporal patterns of variations that define intrinsic neural information.

If, however, the sensitive organism was exposed to large numbers of different and complex electromagnetic patterns from telecommunication systems, computers, and industrial sources, a synergistic electromagnetic environment might emerge. Combinations of higher frequency signals could produce much longer functional pixel durations that would occur in complex sequences. One traditional mechanism to produce these bioeffective pixel durations would be the creation of fields of beats and interference patterns similar to those generated with complex sound fields. If these functional pixel times occurred within the millisecond range and were modulated to contain neural information, they might be accessible by the sensitive brain and influence its electrical activity. The "simplest" information mediated through the centrencephalic and limbic systems might involve emotional arousal or modifications of affective tone.

REFERENCES

CAVALHEIRO, E. A., LEITE, J. P., BORTOLOTTO, Z. A., TURSKI, W. A., IKONOMIDOU, C., & TURSKI, L. (1991) Long term effects of pilocarpine in rats: structural damage of the brain triggers kindling and spontaneous recurrent seizures. *Epilepsia*, 32, 778-782.

KELSO, J. A. S. (1995) *Dynamic patterns*. Cambridge, MA MIT Press.

KOESTER, J. (1991) Passive membrane properties of the neuron. In E. R. Kandel, J. H. Schwartz, & T. M. Jessel (Eds.), *Principles of neural science*. (3rd ed.) New York: Elsevier. Pp. 95-103.

MICHON, A. L., & PERSINGER, M. A. (1997) Experimental simulation of the effects of increased geomagnetic activity upon nocturnal seizures in epileptic rats. *Neuroscience Letters*, 224, 53-56.

PERSINGER, M. A. (1995) Geophysical variables and behavior: LXXIX. Overt limbic seizures are associated with concurrent and premidscotophase geomagnetic activity: synchronization by prenocturnal feeding. *Perceptual and Motor Skills*, 81, 83-93.

PERSINGER, M. A., BUREAU, Y. R. J., KOSTAKOS, M., PEREDERY, O., & FALTER, H. (1993) Behaviours of rats with insidious multifocal brain damage induced by seizures following single peripheral injections of lithium and pilocarpine *Physiology and Behavior*, 53, 849-866.

RACINE, R. J. (1972) Modification of seizure activity by electrical stimulation: II. Motor seizures. *Electroencephalography and Clinical Neurophysiology*, 32, 281-294.

RICHARDS, P. M., PERSINGER, M. A., & KOREN, S. A. (1993) Modification of activation and evaluation properties of narratives by weak complex magnetic field patterns that simulate limbic burst firing. *International Journal of Neuroscience*, 71, 71-85.

THOMAS, A. W., KAVALIERS, M., PRATO, F. S., & OSSENKOPP, K-P. (1997) Antinociceptive effects of pulsed magnetic fields in the land snail *Cepaea nemoralis*. *Neuroscience Letters*, 22, 107-110.

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